The prognostic value of a trend in modified SOFA score forpatients with hematological malignancies in the intensivecare unit

Demandt, Astrid M. P.; Geerse, Daniel A.; Janssen, Bram J. P.; Winkens, Bjorn; Schouten, Harry C.; van Mook, Walther N. K. A.

Published in:
European Journal of Haematology

DOI:
10.1111/ejh.12919

Accepted: 20 June 2017

DOI: 10.1111/ejh.12919

ORIGINAL ARTICLE

WILEY European Journal of Haematology

The prognostic value of a trend in modified SOFA score for patients with hematological malignancies in the intensive care unit

Astrid M.P. Demandt[1] | Daniël A. Geerse[2] | Bram J.P. Janssen[3] | Bjorn Winkens[4] | Harry C. Schouten[1] | Walther N.K.A. van Mook[5]

[1]Division of Hematology, Department of Internal Medicine, GROW, Maastricht University Medical Center, Maastricht, The Netherlands

[2]Division of Nephrology, Department of Internal Medicine, Bravis Hospital, Roosendaal, The Netherlands

[3]Department of Anaesthesiology, University Medical Center Groningen, Groningen, The Netherlands

[4]Department of Methodology and Statistics, CAPHRI, Maastricht University, Maastricht, The Netherlands

[5]Department of Intensive Care Medicine, Maastricht University Medical Center, Maastricht, The Netherlands

Correspondence
Astrid M.P. Demandt, Division of Hematology, Department of Internal Medicine, Maastricht University Medical Center, Maastricht, The Netherlands.
Email: a.demandt@mumc.nl

Abstract

Background: Patients with hematological malignancies admitted to an intensive care unit (ICU) have a poor prognosis. The Sequential Organ Failure Assessment (SOFA) score is used to monitor patients on the ICU. Little is known about the value of this score in hematology patients. Therefore, the prognostic value of the SOFA score and a modified hematological SOFA score (SOFAhem) was studied.

Methods: Patients with hematological malignancies admitted to the ICU between 1999 and 2009 were analyzed in a retrospective cohort study. The SOFAhem score was defined as the original SOFA score omitting the coagulation and neurological parameters.

Results: In 149 admissions, ICU mortality was 52%. Mortality was significantly associated with higher SOFA and SOFAhem scores on admission, and trend in SOFAhem scores. An unchanged and increased SOFAhem score compared to decreasing SOFAhem scores was associated with a higher mortality rate (53% resp 67% resp 25%).

Conclusions: Trends in SOFA or SOFAhem score are both suitable as prognostic parameter. The trend in SOFAhem score seems to be independently related to mortality in hematological patients admitted to the ICU, and because of the higher odds ratios and lower *P*-values compared to the SOFA score, it is probably stronger related to mortality than the classical score, but its prognostic value should be tested in a larger cohort.

KEYWORDS

hematological, intensive care, prognosis, sequential organ failure assessment

1 | INTRODUCTION

Outcome in patients with a hematological malignancy has improved over the last decades thanks to developments in therapeutic options, such as intensive chemotherapy regimens, use of novel agents like targeted drugs and stem cell transplantation on the one, and improvement of supportive measures on the other hand.[1] Concurrently, the incidence of life-threatening complications of these therapies has increased as well, often requiring transfer to an intensive care unit (ICU).[2] Patients with a hematological malignancy admitted to an ICU are often assumed to have a poor prognosis, [3] with reported ICU mortality ranging from 34% to 68%.[3–13] Factors contributing to the prognosis of patients with hematological malignancies admitted to an ICU have been investigated by multiple studies. Most of these found that short-term prognosis is mainly determined by severity of illness, but not by the underlying disease itself or the indication for ICU

TABLE 1 SOFA score

SOFA score	1	2	3	4
Respiration[a]				
PaO_2/FiO_2 mm Hg	<400	<300	<200 with respiratory support	<100 with respiratory support
Coagulation				
Platelets×10^3/mm^3	<150	<100	<50	<20
Liver[a]				
Bilirubin, mg/dL (μmol/L)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (>204)
Cardiovascular[a]				
Hypotension	MAP<70 mm Hg	Dopamine≤5 or Dobutamine (any dose)	Dopamine<5 or (nor) epinephrine≤0.1	Dopamine>1.5 or (nor) epinephrine>0.1
Central nervous system				
Glasgow coma score	13-14	10-12	6-9	<6
Renal[a]				
Creatinine, mg/dL (μmol/L) or urine output	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440) or <500 mL/d	>5.0 (>440) or <200 mL/d

SOFA, sequential organ failure assessment.
J. Vincent Intensive Care Medicine 1996.
[a]Included in $SOFA_{hem}$.

admission.[14] Severity of illness was mainly reflected by higher organ failure scores and the need for mechanical ventilation and vasopressors. This associated poor outcome sometimes results in reluctance to admit this subgroup of patients to the ICU. More recent studies however show a better survival after ICU admission and, even more important, that the long-term health-related quality of life (HRQoL) is not affected.[11,15,16]

It is difficult to predict a patient's prognosis based solely on parameters that are available at ICU admission. For this reason, less restrictive admission policies have been advocated, often resulting in a trial of ICU admission and treatment, during which unlimited care is provided for a limited period of time.[17,18] After an arbitrary period of 3-7 days, a decision is then made whether or not to continue ICU treatment. Consequently, after a few days of ICU treatment there is a need for parameters which contribute to evaluate the prognosis at that time. For this purpose, changes in organ failure scores, such as the Sequential Organ Failure Assessment (SOFA) score[19] (Table 1), during ICU stay have been studied.[3,10,20]

The SOFA score was initially designed to study organ failure in patients with sepsis (sepsis-related organ failure assessment) admitted to the intensive care unit, using six categories (see Materials and Methods). As the score was not specific for sepsis, it was later changed into the Sequential Organ Failure Assessment. A recent study developed a modified hematological SOFA score taking into account recent infection before admission, and this modified score was better for discriminating survivors from non-survivors than the unmodified score.[21]

For several reasons, we hypothesize that the conventional SOFA score is not a good reflection of the current problem that caused the transfer to the ICU. First, as platelets are an important part of the SOFA score, it can be envisaged that the thrombocytopenia in patients with a hematological malignancy admitted to the ICU is an expression of the underlying hematological disease rather than a reflection of the current problem. Second, recent studies evaluated a modified SOFA score in medical and surgical patients, omitting the neurological score and showed this score was significantly associated with mortality.[22,23] The neurological score was excluded as the results of the neurological evaluation are most commonly influenced by the use of sedatives. The recent study in hematological patients only calculated the modified score on admission and because of that we did not involve this score.[21]

In the present study, the classical SOFA score was consequently changed into the modified hematological SOFA score ($SOFA_{hem}$), omitting the coagulation and central nervous system parameters (Table 1), and furthermore the trend in SOFA was studied in a larger cohort because the study of Geerse et al.[10] suggested that the change in SOFA score during the stay on the ICU could be helpful in decision-making about further treatment. We also studied the trend in $SOFA_{hem}$.

2 | MATERIALS AND METHODS

All patients with hematological malignancies that were admitted to the ICU of the Maastricht University Medical Center (MUMC) in Maastricht, the Netherlands, were retrospectively included between December 1999 and November 2009. A cohort of patients previously studied was part of this population.[10] All hematological patients who were transferred from the hematology ward to the ICU or hematological patients who were directly admitted to the ICU through the emergency department were identified. Readmissions were not evaluated. Decisions to admit a patient to the ICU were made together by the intensivists and hematologists.

Because of the retrospective design of the study, approval of the study, by the institutional review board (IRB), was not needed.

The following data were documented: demographic characteristics; type and status of hematological malignancy; therapy characteristics and therapy-related complications, such as the presence and duration of neutropenia and graft-vs-host disease; indication for ICU admission; clinical and laboratory parameters; the need for cardiopulmonary resuscitation, mechanical ventilation, vasopressor/inotropic drugs, and renal replacement therapy; the presence of bacteremia. Using these data, the Acute Physiology And Chronic Health Evaluation II (APACHE II) score was calculated, as well as the Sequential Organ Failure Assessment (SOFA) and modified $SOFA_{hem}$ score on days 1, 3, 5, and 7 after admission. The original SOFA (Table 1) score includes parameters on six organ systems (respiratory, cardiovascular, neurological, hepatic, renal, and coagulation system, respectively, PaO_2, hypotension, Glasgow coma score, bilirubin, creatinine, and platelets).[19] The $SOFA_{hem}$ score was defined as the sum of the four components omitting the coagulation and neurological parameters.

Patients were grouped based on trend in SOFA and $SOFA_{hem}$ score (decreased, increased, or unchanged), with decrease and increase defined as ≥2 points change. The trend in SOFA and $SOFA_{hem}$ score was only calculated between day 1 and day 3, because of a decrease of data availability over time due to transfer back to the hematology ward or death.

Disease status was based on the last available bone marrow biopsy or imaging data and was classified as previously untreated disease, partial or complete remission or progressive disease. Neutropenia was defined as an absolute neutrophil count<0.5×10^9/L.

Continuous variables were expressed as mean±standard deviation or median and interquartile range (IQR). Categorical variables were expressed as total numbers and percentages. To investigate the difference in patient characteristics between ICU survivors and non-survivors, or between time-periods (1999-2004 vs 2005-2009), Pearson's Chi-square or Fisher's exact test for categorical variables and independent samples *t* test or Mann-Whitney *U* test for continuous variables were used where appropriate. The effect of well-known factors associated with ICU mortality and statistically significant differences between ICU survivors and non-survivors were assessed using univariable logistic regression analysis. Using multivariable logistic regression analyses, the effect of the trend in SOFA and in $SOFA_{hem}$ on ICU mortality was corrected separately for invasive mechanical ventilation, vasopressor/inotropic medication, and APACHE II, which are the most important risk factors for ICU mortality.[14] All analyses were performed with IBM SPSS Statistics for Windows (Version 22.0.0; IBM Corp, Armonk, NY, USA). *P*-values≤.05 were considered statistically significant.

3 | RESULTS

In this study, 174 admissions were seen in 149 different patients. Of these, 75 patients (86 admissions) were previously described in the study of Geerse et al.[10] Nineteen patients were readmitted once, three were readmitted twice. Of those patients, only the first admission was evaluated. Table 2 provides baseline characteristics divided by ICU survival. Mean age at ICU admission was 54±13 year, and 92 patients (62%) were male. Median duration of ICU stay was 4 days (IQR 2-10 days). ICU mortality was 52%, and in-hospital mortality was 60%. Mortality after 1 year was 71%. ICU mortality improved slightly over time, being 56% from 1999 to 2004 and 50% from 2005 to 2009. The mean APACHE II scores for the two groups on admission were equal (29±7.8 vs 29±7.1).

Acute myeloid leukemia was the most common hematological malignancy diagnosed (40%), followed by non-Hodgkin lymphoma (31%). In 101 patients (68%), chemotherapy was administered within 30 days prior to ICU admission and 60 patients (40%) had undergone a stem cell transplantation and the majority (60%), an allogeneic transplantation. Neutropenia at ICU admission was seen in 84 patients (56%). The most common indications for ICU admission were respiratory insufficiency (47% of patients) and sepsis (26% of patients). Mean APACHE II score was 29.5±7.4, and mean SOFA score at admission was 10.9±3.4. Ninety-eight patients (66%) were mechanically ventilated and 99 patients (66%) received vasopressor or inotropic therapy within 24 hours after ICU admission.

Differences in ICU survivors and non-survivors are displayed in Table 3. ICU survivors had significantly lower APACHE II scores (26.3±6.5 vs 32.4±6.9), SOFA scores (9.5±3.2 vs 12.2±3.2), and $SOFA_{hem}$ scores at admission (6.3±2.5 vs 8.1±2.5). These differences were also seen for maximum SOFA score (10.4±3.4 vs 14.0±3.3) and maximum $SOFA_{hem}$ score (6.8±2.7 vs 9.2±2.7) during the first week of ICU stay. Vasopressor/inotropic therapy, mechanical ventilation, and bacteremia were more common in ICU non-survivors, as well as the need for resuscitation. These were also statistically significant.

The indication for ICU admission, type of underlying disease, and disease status did not differ between ICU survivors and non-survivors; neither did the presence and duration of neutropenia, neutropenia recovery on the ICU, and the presence of graft- vs -host disease.

SOFA scores were available on day 1 and day 3 for 103 patients. The trend in SOFA and $SOFA_{hem}$ is shown in Table 3. Patients with an unchanged or increased SOFA score had a higher ICU mortality (57 resp. 55%) as compared to patients with a decreased SOFA score (30%). For the patient group with an increased score, this difference was not significant, and for the patients with an unchanged score, it was significant. The $SOFA_{hem}$ showed that patients with an increased score had the highest mortality (67%), but patients with an unchanged $SOFA_{hem}$ score also had a significantly worse outcome (53%) than patients with a decreased $SOFA_{hem}$ score (25%, Table 3).

Table 4 shows the univariable logistic regression analysis of factors associated with ICU mortality. Patients without the history of a stem cell transplantation and patients with an allogeneic stem cell transplantation had significantly higher ICU mortality compared to autologous transplantation. The APACHE II score, the SOFA score at admission and an unchanged SOFA score, and an increased or an unchanged $SOFA_{hem}$ score were also significantly associated with ICU mortality. Furthermore, mechanical ventilation, cardiopulmonary resuscitation,

TABLE 2 Patient characteristics and variables and ICU mortality

Patient characteristics	Total (n=149)		ICU survivors (n=72; 48%)		ICU non-survivors (n=77; 52%)		ICU mortality (%)	*P*-value
Age (mean±SD)	54±13		54±13		54±13			.83
Gender								
Male	92	62%	47	65%	45	58%	49	.41
Female	57	38%	25	35%	32	42%	56	
Hematological malignancy								
Acute leukemia	60	40%	23	32%	37	48%	62	.15
(non)Hodgkin lymphoma	46	31%	25	35%	21	27%	46	
Other	43	29%	24	33%	19	25%	44	
Disease status								
Previously untreated	54	36%	28	39%	26	34%	48	.69
Partial/complete remission	64	43%	31	43%	33	43%	52	
Progressive/refractory	31	21%	13	18%	18	23%	58	
CT in last 30 d								
Yes	101	68%	51	71%	50	65%	50	.49
No	48	32%	21	29%	27	35%	56	
Stem cell transplantation (SCT)								
No	89	60%	42	58%	47	61%	53	.07
Autologous	24	16%	17	24%	7	9%	29	
Non-myeloablative allogeneic	18	12%	7	10%	11	14%	61	
Myeloablative allogeneic	18	12%	6	8%	12	16%	67	
Days between last CT and ICU admission (median, IQR)	12 (2-30)		13 (2-25)		12 (3-48)			.88
Neutropenia on ICU admission								
Yes	84	56%	38	53%	46	60%	55	.41
No	65	44%	34	47%	31	40%	48	
Neutropenia >21 d on ICU admission								
Yes	22	26%	11	29%	11	24%	50	.63
No	62	74%	27	71%	35	76%	56	
Indication for ICU admission								
Respiratory failure	70	47%	32	44%	38	49%	54	.22
Sepsis	38	26%	17	24%	21	27%	55	
Heart failure	15	10%	9	12%	6	8%	40	
Postresuscitation	11	7%	3	4%	8	10%	73	
Neurological	6	4%	4	6%	2	3%	33	
Other	9	6%	7	10%	2	3%	22	
Graft- vs -host disease								
Yes	20	13%	8	11%	12	16%	60	.48
No	129	87%	64	89%	65	84%	50	
Organ failure scores								
APACHE II (mean±SD)	29.5±7.4		26.3±6.5		32.4±6.9			<.001
SOFA score day 1 (mean±SD)	10.9±3.4		9.5±3.2		12.2±3.2			<.001
$SOFA_{hem}$ day 1 (mean±SD)	7.2±2.6		6.3 ±2.5		8.1 ±2.5			<.001
SOFA max in first week (mean±SD)	12.2±3.8		10.4±3.4		14±3.3			<.001
$SOFA_{hem}$ max in first week (mean±SD)	8.1±2.9		6.8±2.7		9.2±2.7			<.001

(Continues)

TABLE 2 (Continued)

Patient characteristics	Total (n=149)		ICU survivors (n=72; 48%)		ICU non-survivors (n=77; 52%)		ICU mortality (%)	*P*-value
Any SOFA score >15 in first week								
Yes	44	30%	12	17%	32	43%	73	<.001
No	103	70%	60	83%	43	57%	42	
Any $SOFA_{hem}$ score >7 in first week								
Yes	104	70%	39	54%	65	86%	62	<.001
No	44	30%	33	46%	11	14%	25	
Invasive mechanical ventilation								
Yes	98	66%	33	46%	65	84%	66	<.001
No	51	34%	39	54%	12	16%	24	
Vasopressor/inotropic medication								
Yes	99	66%	30	42%	69	90%	70	<.001
No	50	34%	42	58%	8	10%	16	
Renal replacement therapy								
Yes	21	14%	7	10%	14	18%	67	.16
No	128	86%	65	90%	63	82%	49	
Bacteriemia								
Yes	56	38%	21	29%	35	46%	63%	.04
No	93	62%	51	71%	42	54%	45%	
Resuscitation								
Yes	25	17%	3	4%	22	29%	88%	<.001
No	124	83%	69	96%	55	71%	44%	
ICU duration (days, median [IQR])	4 (2-10)		4 (1-13)		4 (2-9)			.29

SCT, stem cell transplantation; CT, chemotherapy; IQR, interquartile range; $SOFA_{hem}$ max, highest $SOFA_{hem}$ score in first week; APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit; SOFA, sequential organ failure assessment.

and the need for vasopressor/inotropic therapy were associated with worse outcome.

As described before, the trend in SOFA and $SOFA_{hem}$ score was corrected separately for invasive mechanical ventilation, vasopressor/inotropic therapy, and APACHE II. Patients with an unchanged or increased SOFA score had a significant worse outcome than patients with a decreased SOFA score, only when correcting for vasopressor/inotropic medication an increasing score did not show significance. The trend in $SOFA_{hem}$ score was independently associated with mortality (Table 5). In this analysis, the classical and modified score were both associated with poor patient outcome, but the odds ratios for the $SOFA_{hem}$ score were higher and the *P*-values lower.

4 | DISCUSSION

Whereas most previous studies on the prognosis of hematology patients at the ICU only reported on the predictive value of parameters available on ICU admission, the current study also evaluated prognostic parameters after 3 days of ICU treatment using the classical and a modified SOFA score. The main findings of the present study are consecutively discussed in the sections below.

Our findings confirm that the prognosis in hematological patients is primarily determined by severity of illness, rather than underlying disease specific characteristics.[3,24,25] In this study, mortality was also associated with higher organ failure scores on admission, as well as inotropic/vasopressor therapy and mechanical ventilation. Although some studies reported that disease characteristics were not associated with ICU mortality, other studies reported a poor prognosis in patients after allogeneic SCT,[5,26,27] In the present study, a higher mortality was seen in patients who had received an allogeneic SCT prior to ICU admission. This subgroup of patients represented only a minority (24%) of our population, as was the case in other studies.

Patients without a stem cell transplantation compared to patients with an autologous stem cell transplantation also had a worse outcome. This group reflects the patients with acute leukemia, who have a higher mortality rate than patients without leukemia. Some prior studies also described an association between acute myeloid leukemia (AML) and a worse outcome.[28,29] Analysis of aggregated data across multiple institutions may provide more insight into the prognosis of this patient subgroup. Such a national study has recently been performed in the Netherlands, and its results are eagerly awaited (personal communication).

TABLE 3 Effect of trend in SOFA and $SOFA_{hem}$ score on ICU mortality

	Total (n=103)		ICU survivors (n=53; 51%)		ICU non-survivors (n=50; 49%)		ICU mortality (%)	*P*-value
Trend in SOFA								
Decreased	30	29%	21	40%	9	18%	30	
Unchanged	44	43%	19	36%	25	50%	57	.03
Increased	29	28%	13	24%	16	32%	55	.07
Trend in $SOFA_{hem}$								
Decreased	28	27%	21	40%	7	14%	25	
Unchanged	51	50%	24	45%	27	54%	53	.02
Increased	24	23%	8	15%	16	32%	67	.005

Trend: decreased or increased was defined as ≥2 points change compared to the admission SOFA/$SOFA_{hem}$ score and the SOFA/$SOFA_{hem}$ score on day 3; n.s., non-significant; ICU, intensive care unit; SOFA, sequential organ failure assessment.

TABLE 4 Univariable analysis of factors associated with ICU mortality

	Odds ratio	95% CI	*P*-value
Stem cell transplantation (SCT)			
Autologous	1		
No	2.72	1.03-7.20	.04
Non-myeloablative allogeneic	3.82	1.05-13.91	.04
Myeloablative	4.86	1.30-18.13	.02
Invasive mechanical ventilation	6.40	2.96-13.84	<.001
Bacteriemia	2.02	1.03-3.99	.04
Vasopressor/inotropic medication	12.08	5.06-28.80	<.001
Renal replacement therapy	2.06	0.78-5.45	.14
Resuscitation	9.20	2.62-32.34	<.001
APACHE II	1.15	1.08-1.23	<.001
SOFA score day 1	1.31	1.16-1.47	<.001
$SOFA_{hem}$ day 1	1.33	1.15-1.54	<.001
SOFA max in first week	1.39	1.23-1.57	<.001
$SOFA_{hem}$ max in first week	1.39	1.21-1.60	<.001
Trend in SOFA score between day 1 and 3			
Decreased	1		
Increased	2.87	0.99-8.37	.05
Unchanged	3.07	1.15-8.20	.03
Trend in $SOFA_{hem}$ score between day 1 and 3			
Decreased	1		
Increased	6	1.80-20.02	.04
Unchanged	3.38	1.22-9.33	.02
ICU duration	1	0.99-1.01	.99
Disease status			
Partial or complete remission	1		
Previously untreated	0.87	0.42-1.8	.71
Progression (refractory and relapse)	1.30	0.55-3.09	.55
Chemotherapy in last 30 d	0.76	0.38-1.52	.44
Graft- vs -host disease	1.48	0.57-3.86	.43
Neutropenia on ICU admission	1.30	0.69-2.54	.39

CI, confidence interval; APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit; SOFA, sequential organ failure assessment.

TABLE 5 Multivariable logistic regression analyses for trend in $SOFA_{hem}$ and SOFA score corrected for consecutively APACHE, invasive mechanical ventilation (MV), and vasopressor/inotropic medication (INO)

	Odds ratio	95% CI	*P*-value		Odds ratio	95% CI	*P*-value
APACHE	1.21	1.10-1.33	<.001	APACHE	1.17	1.08-1.27	<.001
Trend in $SOFA_{hem}$				Trend in SOFA			
Decreasing	1			Decreasing	1		
Increasing	17.64	3.74-83.13	<.001	Increasing	5.77	1.63-20.48	.007
Stable	7.88	2.18-28.48	.002	Stable	4.68	1.50-14.63	.008
MV	5.69	2.10-15.45	.001	MV	5.25	1.97-13.97	.001
Trend in $SOFA_{hem}$				Trend in SOFA			
Decreasing	1			Decreasing	1		
Increasing	8.02	2.19-29.42	.002	Increasing	3.95	1.24-12.59	.02
Stable	4.6	1.55-13.68	.006	Stable	3.65	1.29-10.37	.015
INO	18.18	5.23-63.17	<.001	INO	15.97	4.76-53.60	<.001
Trend in $SOFA_{hem}$				Trend in SOFA			
Decreasing	1			Decreasing	1		
Increasing	6.06	1.59-23.06	.008	Increasing	2.75	0.83-9.14	.099
Stable	6.11	1.86-20.11	.003	Stable	4.2	1.33-13.29	.015

MV, invasive mechanical ventilation; INO, vasopressor/inotropic medication; APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment.

In line with most other studies, no difference in mortality in patients with neutropenia or patients with neutropenia recovery during ICU stay was seen. Some studies, although, did find higher mortality in patients with neutropenia or neutropenia recovery at the ICU.[30,31]

Furthermore, the change in SOFA score offers important additional prognostic information to help in this decision-making process to continue or discontinue treatment during such an ICU trial.[3,8,10] Patients with a deterioration of SOFA or $SOFA_{hem}$ score have a poor prognosis, and the trend in SOFA and $SOFA_{hem}$ score is independently related to mortality in our population of hematological patients admitted to the ICU.

The observation that the odds ratios for the $SOFA_{hem}$ score are higher than for the SOFA score in the multivariable analysis and the *P*-values are lower even supports our view that the $SOFA_{hem}$ score was stronger related with mortality than the classical SOFA score. In hematological patients, neither the coagulation nor the neurological parameters are thus contributive because thrombocytopenia does not have to be an expression of the severity of illness, but is likely to be at least partly, an expression of the underlying hematological disease.

The conclusions of other studies that the neurological component can also be omitted were confirmed in this patient group.[22,23]

Despite the improvement in predictive power using the $SOFA_{hem}$ score compared to the traditional SOFA score, the trend in $SOFA_{hem}$ score is however still not an absolute decisive factor whether to continue treatment or not, as even in the poor risk group with an increasing $SOFA_{hem}$ score, about 30% of the patients survive their intensive care stay. However, the trend in $SOFA_{hem}$ score can aid in decision-making, taking into account all other clinically relevant information, and seems to perform better than the traditional SOFA in this respect.

5 | LIMITATIONS

This study has some limitations. First, this is a retrospective single center study. Admission policies and decision-making regarding resuscitation may be center specific, so patient characteristics in our population may differ from other centers. This may decrease the generalizability of our findings.

Second, in a significant number of patients (46/149), data to calculate the $SOFA_{hem}$ score on day 3 were not available, either due to missing results, death of the patients, or discharge to the ward before a second SOFA score could be determined. Therefore, the SOFA trend could not be analyzed for all included patients.

Third, our population included patients with a mix of different hematological diseases. Conclusions may be different for certain subgroups. These subgroups were too small to perform multivariable analysis.

6 | CONCLUSIONS

In patients with hematological malignancies admitted to the ICU, trends in SOFA or $SOFA_{hem}$ score are both suitable as prognostic parameters that could aid in decision-making regarding continuation of care. In this study, an unchanged or increased $SOFA_{hem}$ and unchanged SOFA score between days 1 and 3 is independently associated with mortality in ICU patients with hematological malignancies. The trend in the modified hematological SOFA score omitting the neurological and hematological component probably is stronger related to mortality compared to the classical score and can be used in daily practice. It seems promising as an independent predictor of

mortality in our population of hematological patients admitted to the ICU. Further large prospective studies are needed to confirm these preliminary findings.

CONFLICT OF INTEREST

All authors declare to have no conflict of interest.

REFERENCES

1. Azoulay E, Mokart D, Pene F, et al. Outcomes of critically ill patients with hematologic malignancies: prospective multicenter data from France and Belgium–a groupe de recherche respiratoire en reanimation onco-hematologique study. *J Clin Oncol*. 2013;31:2810-2818.
2. Gordon AC, Oakervee HE, Kaya B, et al. Incidence and outcome of critical illness amongst hospitalised patients with haematological malignancy: a prospective observational study of ward and intensive care unit based care. *Anaesthesia*. 2005;60:340-347.
3. Lamia B, Hellot MF, Girault C, et al. Changes in severity and organ failure scores as prognostic factors in onco-hematological malignancy patients admitted to the ICU. *Intensive Care Med*. 2006;32:1560-1568.
4. Park HY, Suh GY, Jeon K, et al. Outcome and prognostic factors of patients with acute leukemia admitted to the intensive care unit for septic shock. *Leuk Lymphoma*. 2008;49:1929-1934.
5. Thakkar SG, Fu AZ, Sweetenham JW, et al. Survival and predictors of outcome in patients with acute leukemia admitted to the intensive care unit. *Cancer*. 2008;112:2233-2240.
6. Trinkaus MA, Lapinsky SE, Crump M, et al. Predictors of mortality in patients undergoing autologous hematopoietic cell transplantation admitted to the intensive care unit. *Bone Marrow Transplant*. 2009;43:411-415.
7. Roze des Ordons AL, Chan K, Mirza I, Townsend DR, Bagshaw SM. Clinical characteristics and outcomes of patients with acute myelogenous leukemia admitted to intensive care: a case–control study. *BMC Cancer* 2010;10:516.
8. Vandijck DM, Depuydt PO, Offner FC, et al. Impact of organ dysfunction on mortality in ICU patients with hematologic malignancies. *Intensive Care Med*. 2010;36:1744-1750.
9. Villa F, Coppadoro A, Bellani G, Foti G, Fumagalli R, Pesenti A. Etiology of respiratory failure is related to mortality in critically ill patients affected by a hematological malignancy: a retrospective study. *Minerva Anestesiol*. 2010;76:7-12.
10. Geerse DA, Span LF, Pinto-Sietsma SJ, van Mook WN. Prognosis of patients with haematological malignancies admitted to the intensive care unit: sequential organ failure assessment (SOFA) trend is a powerful predictor of mortality. *Eur J Intern Med*. 2011;22:57-61.
11. Bird GT, Farquhar-Smith P, Wigmore T, Potter M, Gruber PC. Outcomes and prognostic factors in patients with haematological malignancy admitted to a specialist cancer intensive care unit: a 5 yr study. *Br J Anaesth*. 2012;108:452-459.
12. Horster S, Stemmler HJ, Mandel PC, et al. Mortality of patients with hematological malignancy after admission to the intensive care unit. *Onkologie*. 2012;35:556-561.
13. Magid T, Haase N, Andersen JS, Nielsen OJ, Bonde J. Intensive care of haematological patients. *Dan Med J* 2012;59(3):A4395.
14. Massion PB, Dive AM, Doyen C, et al. Prognosis of hematologic malignancies does not predict intensive care unit mortality. *Crit Care Med*. 2002;30:2260-2270.
15. Vliet M, Verburg IW, van den Boogaard M, et al. Trends in admission prevalence, illness severity and survival of haematological patients treated in Dutch intensive care units. *Intensive Care Med* 2014;40:1275-1284.
16. Townsend WM, Holroyd A, Pearce R, et al. Improved intensive care unit survival for critically ill allogeneic haematopoietic stem cell transplant recipients following reduced intensity conditioning. *Br J Haemotol*. 2013;161:578-586.
17. Azoulay E, Soares M, Darmon M, Benoit D, Pastores S, Afessa B. Intensive care of the cancer patient: recent achievements and remaining challenges. *Ann Intensive Care*. 2011;1:5.
18. Lecuyer L, Chevret S, Thiery G, Darmon M, Schlemmer B, Azoulay E. The ICU trial: a new admission policy for cancer patients requiring mechanical ventilation. *Crit Care Med*. 2007;35:808-814.
19. Vincent JL, Moreno R, Takala J, et al. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996;22:707-710.
20. Cárdenas-Turanzas M, Ensor J, Wakefield C, et al. Cross-validation of a sequential organ failure assessment score-based model to predict mortality in patients with cancer admitted to the intensive care unit. *J Crit Care*. 2012;27:673-680.
21. Greenberg J, David M, Churpek M, et al. Sequential organ failure assessment score modified for recent infection in patients with hematologic malignant tumors and severe sepsis. *Am J Crit Care*. 2016;25:409-417.
22. Namendys-Silva SA, Silva-Medina MA, Vasquez-Barahona GM, et al. Application of a modified sequential organ failure assessment score to critically ill patients. *Braz J Med Biol Res*. 2013;46:186-193.
23. Nates JL, Cardenas-Turanzas M, Ensor J, et al. Cross-validation of a modified score to predict mortality in cancer patients admitted to the intensive care unit. *J Crit Care*. 2011;26:388-394.
24. Park MR, Jeon K, Song JU, et al. Outcomes in critically ill patients with hematologic malignancies who received renal replacement therapy for acute kidney injury in an intensive care unit. *J Crit Care*. 2011;26:e1-e6.
25. Boyaci N, Aygencel G, Turkoglu M, et al. The intensive care management process in patients with hematopoietic stem cell transplantation and factors affecting their prognosis. *Hematology*. 2014;19:338-345.
26. Afessa B, Azoulay E. Critical care of the hematopoietic stem cell transplant recipient. *Crit Care Clin*. 2010;26:133-150.
27. Pene F, Aubron C, Azoulay E, et al. Outcome of critically ill allogeneic hematopoietic stem-cell transplantation recipients: a reappraisal of indications for organ failure supports. *J Clin Oncol*. 2006;24:643-649.
28. Depuydt PO, Benoit DD, Vandewoude KH, et al. Outcome in noninvasively and invasively ventilated hematologic patients with acute respiratory failure. *Chest*. 2004;126:1299-1306.
29. Bahammam AS, Basha SJ, Masood MI, et al. Outcome of patients with hematological malignancies admitted to the intensive care unit with life-threatening complications. *Saudi Med J*. 2005;26:246-250.
30. Benoit DD, Vandewoude KH, Decruyenaere JM, Hoste EA, Colardyn FA. Outcome and early prognostic indicators in patients with a hematologic malignancy admitted to the intensive care unit for a life-threatening complication. *Crit Care Med*. 2003;31:104-112.
31. Rhee CK, Kang JY, Kim YH, et al. Risk factors for acute respiratory distress syndrome during neutropenia recovery in patients with hematologic malignancies. *Crit Care*. 2009;13:R173.

How to cite this article: Demandt AMP, Geerse DA, Janssen BJP, Winkens B, Schouten HC, Mook WNKAV. The prognostic value of a trend in modified SOFA score for patients with hematological malignancies in the intensive care unit. *Eur J Haematol*. 2017;99:315–322. https://doi.org/10.1111/ejh.12919